6. Nervous System Diseases (including Alzheimer's Disease)

Reference

Matsushita M, Saito M, Katayama S, et al. Clinical evaluation of DS-4773 on sedative effect: a cross-over trial. *Yakuri to Chiryo* (*Japanese Pharmacology & Therapeutics*) 1994; 22: 2371–82 (in Japanese). Ichushi Web ID: 1995083169

1. Objectives

To evaluate the efficacy and safety of DS-4773 for sedation versus sansoninto (酸棗仁湯) used as control.

2. Design

Randomized cross-over controlled trial (RCT-cross over).

3. Setting

The Department of Neurology and Psychiatry, University of Tokyo Hospital, departments of psychiatry of 5 hospitals, and 2 clinics, Japan.

4. Participants

Seventy-nine male and female patients (≥ 15 years old) with medical histories taken by specialists in the fields of internal medicine, psychosomatic medicine, or psychiatry and any of the following five complaints: insomnia, daytime irritability, daytime bad mood, daytime hypobulia, and lack of refreshing sleep.

5. Intervention

Arm 1: oral administration of DS-4773 (containing 0.5 g dried extract of sansonin [酸棗仁], 0.1 g dried extract of bukuryo [茯苓], and 0.2 g of sanshishi [山梔子]) granules 1 sachet (1 g) b.i.d. before breakfast and before bedtime for 2 weeks (n=79).

Arm 2: oral administration of sansoninto (酸棗仁湯) extract granules for medical use (manufacturer unknown) 1 sachet (3.75 g) b.i.d. before breakfast and before bedtime for 2 weeks (n=79).

6. Main outcome measures

Ease of falling asleep, depth of sleep, mood on awakening, daytime mood, daytime physical condition, daytime motivation, anorexia, constipation and diarrhea, rated on a 4-point scale.

7. Main results

After exclusions and withdrawals, 59 patients were included in the analysis population. Slight or more improvement was reported in 63.5%/51.9% of patients (arm 1/arm 2) for ease of falling asleep, 63.6%/45.5% for depth of sleep, 64.9%/50.9% for mood on awakening, 50.0%/37.5% for daytime mood, 47.4%/38.6% for daytime physical condition, 35.8%/26.4% for daytime motivation, 27.8%/23.2% for anorexia, 41.2%/35.3% for constipation, and 100%/75.0% for diarrhea. Group comparison revealed a significant improvement in the ease of falling asleep, depth of sleep, mood on awakening, daytime physical condition, and daytime motivation in arm 1 compared with arm 2.

8. Conclusions

DS-4773 is more efficacious than sansoninto extract granules for sedation.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Safety was evaluated in 68 patients. No adverse reactions were noted in 64 patients receiving DS-4773 (94.1%) and 61 patients receiving sansoninto (89.7%). Adverse reactions requiring treatment discontinuation were palpitations, dizziness, and anxiety, each occurring in 1 patient.

11. Abstractor's comments

This is a well-designed clinical study with a cross-over design. It investigated the efficacy of DS-4773 using sansoninto extract granules as control. However, lack of a washout period between treatments may have resulted in carry-over effects of the first drug. Furthermore, 7 patients receiving DS-4773 and 1 patient receiving the control drug were noncompliant at the time of either inclusion or exclusion after 2 weeks of treatment, suggesting that more participants received DS-4773 first and this may have contributed to the greater efficacy of DS-4773. In the section on concomitant drugs, combinations with hypnotics were used to treat persistent sleep disorder, suggesting that the hypnotic may have improved the efficacy of the investigational product. The contribution of concomitant drugs to the efficacy of DS-4773 should be evaluated to better determine the actual efficacy of this Kampo medicine.

12. Abstractor and date

Goto H, 18 August 2008, 1 June 2010, 31 December 2013.